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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/826,112	04/17/2004	Reuben Matalon	P71641US0	9858

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EXAMINER	
FINN, MEGHAN R	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/826,112	MATALON, REUBEN	
	Examiner	Art Unit	
	MEGHAN FINN	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33 and 35-56* is/are pending in the application.

4a) Of the above claim(s) *1-16 and 41-55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-33, 35-40, and 56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 30, 2009 has been entered.

Applicants' arguments, filed January 30, 2009, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20, 21, and 24-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20 recites the limitation "the weight ratio of leu to val in the LNAA supplement" however there is no valine required in the previous claim or claim 20.

There is insufficient antecedent basis for this limitation in the claim. Claim 21 depends from claim 20 and thus also lacks antecedent basis.

Claim 24-31 recites the limitation "said weight ratio of Leu to iLeu" or "said weight ratio of Leu to Val" in reference to claim 22, however neither Val or iLeu are required in claim 22 and no ratio is mentioned. There is insufficient antecedent basis for this limitation in these claims.

In claims 24, 26, and 28 applicant uses the phrase "greater than about 0.5:1" and this phrase is indefinite. The term "greater than" implies a specific boundary of the lower limit being that value cited, however the term "about" is ambiguous and implies that there is no fixed boundary. Thus one of skill in the art would not be able to determine what values are claimed because it is not clear what the lower limit is and the two terms conflict in their meanings. Thus claims 24, 26, and 28 are rejected for failing to distinctly point out and claim the subject matter which applicant regards as the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 19, 22-26, 28-29, and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Dudrick et al. (US 5,026,721).

In claim 19, applicant claims a LNAA supplement comprising Leu and iLeu, wherein the weight ratio of Leu to iLeu is greater than 3:1. Dudrick et al. teach amino acid compositions containing both Leucine and isoleucine and in Table 1 (column 4, lines 1-22) they teach 10.8-13.8% preferred of leucine and 2.5-3.6% of isoleucine, for a 500mg tablet that would be 54-69mg of leucine and 12.5-18mg of isoleucine, thus Dudrick et al. clearly teaches greater than 3:1 ratio (54mg/18mg is a 3:1 ratio and that is the upper limit of isoleucine to the lower limit of leucine) and thus Dudrick et al. anticipates claim 19.

In claim 22, applicant claims a LNAA supplement comprising one or more LNAAs and further comprising Lys in an amount of 5-30mg per 500mg of supplement. Dudrick et al. teaches lysine at 4.5% (table 1, column 4, lines 1-20) which is 22.5mg which is within the claimed range and thus claim 22 is unpatentable over Dudrick et al.

In claim 23, applicant claims the supplement of claim 22 further comprising Leu, which as discussed above is taught by Dudrick et al. between 54-69mg and thus claim 23 is also anticipated by Dudrick et al.

In claims 24-25, applicant clams the supplement of claim 22 wherein the Leu to iLeu ratio is greater than about 0.5:1 or greater than 3:1, which as discussed above Dudrick et al. teaches ratios of 3:1 or higher of Leu to iLeu and thus anticipates claims 24-25.

In claim 26, applicant claims the ratio of Leu to Val is greater than about 0.5:1. Dudrick et al. teaches 54-69mg of leucine as discussed above and 17.2-30.2% (or 86-

151mg) which is greater than a 0.5:1 ratio (54mg of leucine to 86mg of valine is 0.62:1 ratio). Thus claim 26 is also unpatentable over Dudrick et al.

Claims 28-29 claim the same ratios of Leu to iLeu and Leu to Val as claimed in the above mentioned claims and are also anticipated by Dudrick et al. for the reasons discussed above.

Claim 32 claims the supplement of claim 22, wherein the LNAA supplement is substantially free from phenylalanine. Dudrick et al. teaches some embodiments of their composition contain 0% phenylalanine (table 1, column 4, lines 1-20) and thus Dudrick et al. anticipates claim 32.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 17-33, 35-36, and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wachtel et al. (DE 4037447 A1, translation provided), already of record, for the reasons set forth at pages 3-6 of the office action dated October 15, 2007, and pages 3-5 of the office action dated August 1, 2008, of which reasons are herein incorporated by reference.

Claims 17-33, 35-36, and 56 were previously rejected as anticipated by Wachtel et al. and applicant has argued that the ±10% and ±20% cited in Wachtel et al. are percentages of the percentages rather than a percentage to be added/subtracted from the listed percentages and applicant provided a declaration by Jan Ruud Hansen to that effect. While the examiner still thinks that ±10% (as in 14.5% [4.5%-24.5%]) is a possible interpretation of the prior art, it is perhaps not clear if Wachtel et al. anticipates the ranges due to this disagreement, however even if the smaller ranges (as in 14.5% [13.05%-15.95%]) are used, Wachtel et al. renders claims 17-33, 35-36 and 56 unpatentable.

For claims 22-24, 26, 28, 32-33, and 35-36, Wachtel et al. teaches compositions with the same components at the claimed amounts or "about" those amounts. For claims 22-23, applicant claims a LNAA supplement containing Lys between about 5-30mg per 500mg which further comprises Leu. As shown below in the comparison for claim 33, both Leu and Lys are taught and in amounts "about 5-30mg". The term "about" is functional language and means any amount that performs the same function

is considered about, and is also considered to include values up to 4x those claimed, which would mean that the 65mg taught by Wachtel et al. are "about 30mg". Thus claims 22-23 are unpatentable over Wachtel et al.

In claims 24, 26, and 28 applicant claims the supplement of claim 22, wherein the Leu to iLeu ratio is “greater than about” 0.5:1 (claim 24) and the ratio of Leu to Val is "greater than about" 0.5:1 (claim 26), and claim 28 requires both ratios. The ratios taught by Wachtel et al. are 2:1 Leu/iLeu and 1.7:1 Leu/Val. Both are greater than 0.5:1 and thus claims 24, 26 and 28 are unpatentable over Wachtel et al.

For claim 33, applicant claims specific dosages of the following amino acids, all of which are taught by Wachtel et al, in the amounts listed below. It is noted that the smaller range for the values taught by Wachtel et al. is used.

Applicant’s interpretation of the amounts taught in Wachtel et al:

Amino Acid	LNAA of Claim 33 (mg in 500mg total)	Wachtel et al. (mg in 500 mg total)
Tyrosine	About 100-290	72-88
Tryptophan	About 25-75	14.4-21.6
Methionine	About 15-50	19.6-29.4
Isoleucine	About 15-55	53.6-65.5
Threonine	About 15-50	38-57
Valine	About 15-55	64.8-79.2
Leucine	About 15-200	90.9-111.1
Histidine	About 10-30	20-30
Lysine	About 5-200	65.3-79.8

For Methionine, Isoleucine, Threonine, Leucine, Histidine, and Lysine, Wachtel et al. teaches amounts overlapping with those claimed and those amounts would clearly be obvious in light of those amounts taught by Wachtel et al, even the with the smaller ranges. For Tyrosine, Tryptophan, and Valine the ranges taught by Wachtel et al. do not overlap with the numbers claimed in the instant application, **however** the term "about" as discussed above, is function language and is broad and is interpreted as including amounts up to 4x (plus or minus) the amount claimed. In the case of Tryptophan the difference is only 3.4mg, in Valine the difference is 9.8mg, and in the case of Tyrosine, where the difference is 12mg. All of these differences are well within even 2x the amounts claimed and would obviously be within the limits of routine experimentation for one of ordinary skill in the art. Thus claim 33 is unpatentable over Wachtel et al.

In claims 32 and 35-36 applicant claims that the composition is substantially free of phenylalanine (claims 32, and 36) and arginine (claim 35). Since Wachtel et al. teaches compositions that do not include either of those components as demonstrated by the table shown above for claim 33, it would have been obvious to one of ordinary skill in the art at the time of the invention that the compositions of Wachtel et al. are free of those components and thus claims 32 and 35-36 are unpatentable over Wachtel et al.

In claims 17-21, 25, 27, 29-31, and 56, applicant claims ratios of Leu to Val of greater than 2:1 (claim 17-18, 20-21, 27, 30-31, and 56) and that the ratio of Leu to iLeu

is greater than 3:1 (claims 19, 25, 29, and 31). In the case of Leu to Val, Wachtel et al. teaches 111.1mg of Leucine and 64.8mg of Valine. This is a 1.7:1 ratio, which would reasonably interpreted by one of skill in the art to be rounded to 2:1, and is also sufficiently close to one of ordinary skill in the art at the time of the invention to adjust levels of each amino acid thru routine optimization and it would be obvious that a 2:1 ratio of Leu to Val is within the scope of teachings of Wachtel et al.

For the ratio of Leu to iLeu, Wachtel et al. teaches 111.1mg of Leucine and 53.6mg of isoleucine. This is a 2.07:1 ratio, which would be interpreted as a 2:1 ratio of Leu to iLeu. This is equivalent the 3:1 ratio claimed by applicant, however 16.6mg less of iLeu (or some combination of increased Leu and less iLeu) would produce a 3:1 ratio of Leu to iLeu. This type of minor change in amounts would be within the routine limits of experimentation, and one of ordinary skill in the art at the time of the invention would recognize the similarity of a 2:1 ratio and a 3:1 ratio being within those normal limits of routine experimentation/optimization. Thus both of the ratios claimed by applicant are unpatentable over Wachtel et al. and claims 17-21, 25, 27, 29-31, and 56 are unpatentable over Wachtel et al.

Claims 37-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wachtel et al. (DE 4037447 A1) in view of Ghadimi et al. (US 3,822,465), in further view of Nakaki et al. (Beneficial Circulatory Effect of L-arginine) each already of record, for the reasons set forth at pages 7-9 of the office action dated October 15, 2007, and for

the reasons set forth at pages 5-7 of the final rejection dated August 01, 2008, of which reasons are herein incorporated by reference.

In the previous office action, claims 37-40 were rejected over Wachtel et al. in view of Ghadimi et al., in further view of Nakaki et al. In claim 37, applicant claims a LNAA supplement comprising the amounts of amino acids shown in the table below, with the values taught by Wachtel et al. shown for comparison.

Note the values used for Wachtel et al. are the smaller range discussed above, which applicant maintains as the only acceptable range.

Amino Acid	LNAA of Claim 37 (mg in 600mg total)	Wachtel et al. (mg in 600 mg total)
Tyrosine	About 100-290	86.4-105.6
Tryptophan	About 30-90	17.3-25.9
Methionine	About 25-75	23.5-35.3
Isoleucine	About 15-45	64.3-78.5
Threonine	About 15-50	45.6-68.4
Valine	About 15-50	77.8-95.0
Leucine	About 40-200	109.1-133.3
Histidine	About 15-45	24-36
Arginine	About 15-50	0, 26.6-53.3mg. taught by Ghadimi et al.

For Tyrosine, Methionine, Threonine, Leucine, and Histidine the values of Wachtel et al. overlap those claimed. For Arginine, this amino acid is not taught by Wachtel et al., however the dosage taught by Ghadimi et al. overlaps with that claimed.

For Tryptophan, Isoleucine, and Valine the values taught by Wachtel et al. do not overlap with those claimed, however the term "about" as discussed above is broad and can encompass up to 4x (or 1/4th) of the claimed value. Differences of 4.1mg for Tryptophan, 19.3 mg for isoleucine, and 27.8mg for valine are larger than the differences for claim 33, however they are well within the limits of even 2x (1/2) the values claimed, and small enough that they would be well within the limits of routine optimization. Thus the amounts claimed are obvious over Wachtel et al. and Ghadimi et al. As far as the motivation to add Arginine to the composition, this was addressed in the previous office actions, but to summarize Nakaki et al. teaches that arginine is an essential amino acid and is necessary to supplement to growing children (abstract). Applicant has argued that Nakaki et al. does not teach treatment of PKU, and the examiner apologizes if applicant was given the impression that that was the examiner's argument, however it was not. Nakaki et al. provides the motivation to add Arginine to the composition of Wachtel et al. because it is an essential amino acid that children cannot synthesize and would be beneficial for treatment of children with PKU to combine both the compounds in Wachtel et al. with the arginine taught by Nakaki et al. for one supplement. Ghadimi et al. is relied upon to show that amounts/dosages of 26-50mg were known in the art and even for similar nutritional supplement containing many of the same amino acids. The applicant is incorrect in asserting however that it would not be obvious to combine the arginine with the composition of Wachtel et al. because the composition of Ghadimi contains compounds that are harmful for the treatment of PKU. This was never suggested as one of skill in the art would add arginine to the

composition of Wachtel et al., not Ghadimi et al. Thus claim 37 is unpatentable over Wachtel et al. in view of Ghadimi et al. in further view of Nakaki et al.

Claims 38 claims that the supplement of claim 37 further comprises lysine, which is taught by Wachtel et al. as discussed above and is therefore unpatentable over Wachtel et al. in view of Ghadimi et al. in further view of Nakaki et al.

In claim 39, applicant claims about 5 to about 200mg of lysine. As discussed above Wachtel et al. teaches 65.3-79.8mg of lysine and thus claim 39 is also unpatentable over Wachtel et al. in view of Ghadimi et al. in further view of Nakaki et al.

In claim 40, applicant claims that the composition is free of phenylalanine, and as discussed above since the composition of Wachtel et al. is free of phenylalanine, and it would be harmful to one being treated for PKU as taught by Wachtel et al. it would be obvious to keep the composition free of phenylalanine. Thus claim 40 is also unpatentable over Wachtel et al. in view of Ghadimi et al. in further view of Nakaki et al.

Applicant has made the additional argument that Ghadimi et al. teaches amino acid compositions for intravenous administration and that applicant's invention is enteral or oral administration and that one would not have thought the compositions of Ghadimi et al. were suitable for oral or enteral use. Firstly, applicant has not **claimed** any formulation with specific administration routes. The claims do not require oral or enteral administration or that the compounds are suitable for such. Additionally, Ghadimi et al. is relied upon to provide a starting dosage for optimization and is not relied upon for administration methods.

This argument was carefully considered however is not deemed persuasive and thus the rejection of claims 37-40 is **maintained.**

Conclusion

No claims are allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Meghan Finn whose telephone number is (571) 270-3281. The examiner can normally be reached on 9:30am-7pm Mon-Thu, 9:30am-6pm Friday (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Meghan Finn

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614